8EHQ-96-13626
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8EHQ-0496-15626

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April 10, 1996

(A)

CERTIFIED MAIL
RETURN RECEIPT REQUESTED
P 253 155 648

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OPPT NCIC
96 APR 22 AM 11:35

OPPT Document Processing Center (7407)
ATTN: Section 8(e) Coordinator
Office of Pollution Prevention and Toxics (OPPT)
US Environmental Protection Agency
Washington, DC 20460

RE: TSCA Section 8(e) Notice

Dear Sir or Madam:

This notice is being submitted by Rhône-Poulenc Ag Company (RPAC) to the Environmental Protection Agency (EPA) in accordance with the provisions of Section 8(e) of the Toxic Substances Control Act (TSCA), 15 USC § 2607 (e).

We are submitting results on a variety of compounds from the same chemical family that are being screened for research and development purposes. Only limited quantities of these compounds have been synthesized.

RPAC claims the alpha-numeric designations and the specific chemical identities of the substances at issue to be confidential business information (CBI). The chemical substances may be nonconfidentially identified as a "heterocycles".

In one type of screening study involving repeated dosing, groups of five male mice were administered a test substance suspended in corn oil as follows:

10 mg/kg/day on Days 1 to 4
20 mg/kg/day on Days 5 to 8
40 mg/kg/day on Days 9 to 12

Surviving animals were sacrificed three days after the last dose administered on Day 12. Information on the following compounds is being submitted based on the observation of clinical signs on several occasions in several animals or increased liver weights. Most animals died within a few days of exhibiting clinical signs. However, in a few instances, animals displaying clinical signs survived until study termination.

: All mice survived to study termination and no clinical signs were reported. Absolute liver weight was increased 113% above control. KS

8/5/96

_____: All mice died. Mice were found dead on Days 8, 11, 12, 13, and 15. The mouse found dead on Day 8 exhibited prostration and was cold to touch on Days 7 and 8. This mouse also exhibited palpebral ptosis and tremors on Day 8. The mouse found dead on Day 12 exhibited reduced motor activity and was cold to touch on Days 10 and 11. This mouse also exhibited prostration and palpebral ptosis on Day 11. The mouse that was found dead on Day 13 exhibited reduced motor activity on Days 11 and 12 and hunched posture, piloerection, dyspnea, and was cold to touch on Day 12. The mouse found dead on Day 15 exhibited staggering step and reduced motor activity on Days 12, 13, and 14, and piloerection, hunched posture, and palpebral ptosis on Days 13 and 14.

_____: All mice died. Mice were found dead on Days 6, 7, 10, 13, and 14. The mouse found dead on Day 6 exhibited convulsions on the day of death. The mouse found dead on Day 7 exhibited prostration and was cold to touch on Day 6. The mouse that was found dead on Day 10 exhibited reduced motor activity and piloerection on Days 8 and 9 and was cold to touch on Day 9. The mouse that was found dead on Day 13 exhibited reduced motor activity, dyspnea, staggering step and was cold to touch on Day 13. The mouse that was found dead on Day 14 exhibited reduced motor activity on Days 7 through 13, piloerection and staggering step on Days 8 through 13, was cold to touch on Days 10 through 13, and showed hunched posture on Day 13.

_____: Two of five mice died. Excessive jumps were observed in one mouse on Days 12, 13, and 14. Another mouse exhibited increased motor activity on Days 5 and 9, reduced motor activity during Days 6 through 12, hunched posture on Days 6 and 7, dyspnea on Days 10 through 13, prostration on Day 13 and was cold to touch on Days 10 through 13. This mouse died on Day 14. The mouse found dead on Day 12 exhibited hunched posture on Days 9, 10, and 11 and reduced motor activity on Day 11.

_____: One of five mice died. This mouse was found dead on Day 15 and exhibited piloerection, hunched posture, and palpebral ptosis on Day 12, 13, and 14. One animal surviving to study termination exhibited writhing, reduced motor activity, and piloerection on Days 13 and 14. No clinical signs were reported for the other three mice.

_____: All mice survived to study termination. One mouse exhibited piloerection on Days 11 through 14. Another mouse exhibited irritability to touch on Days 9 and 10, hunched posture and piloerection on Days 12, 13, and 14, and prostration and tremors on Days 13 and 14.

_____: All mice died. Mice were found dead on Days 3, 4, 5, 6, and 9. The mouse found dead on Day 4 exhibited irritability to touch on Day 3. The mouse found dead on Day 5 exhibited reduced motor activity on Days 3 and 4 and palpebral ptosis and piloerection on Day 4. The mouse that was found dead on Day 9 exhibited piloerection and hunched posture on Days 6, 7, and 8 and was cold to touch on Days 7 and 8.

_____: One mouse was found dead on Day 12 after being found prostrate and cold to touch on Day 11. All other mice survived to study termination. One of the surviving mice exhibited increased motor activity and irritability to touch on Day 12. Absolute liver weight was increased 119% above control.

_____: All mice survived to study termination and no clinical signs were reported. Absolute liver weight was increased 151% above control.

_____: All mice survived to study termination and no clinical signs were reported. Absolute liver weight was increased 128% above control.

In another type of screen, a single bolus dose of 100 mg/kg was administered by gavage to five fasted male mice on Study Day 1. Mice were observed daily for clinical signs of toxicity and mortality, and any surviving animals were sacrificed 14 days after dosing. Information on the following compounds is being submitted based on the observation of clinical signs on several occasions in several animals. Most animals died within a few days of exhibiting clinical signs. However, in a few instances, animals displaying clinical signs survived until study termination.

_____: Two mice were found dead, one on Day 8 and the other on Day 10. The mouse found dead on Day 8 was prostrate and cold to touch on Day 7. No clinical signs were reported for the mouse found dead on Day 10. Three mice surviving to study termination exhibited reduced motor activity, staggering step, piloerection, or prostration on several days.

_____: One mouse died. Several mice exhibited reduced motor activity, prostration, hunched posture, piloerection, and staggering step for several days.

_____: All mice survived to study termination. Tremors, piloerection, and hunched posture were observed in one mouse on Day 1. Polypnea and tremors were observed in another mouse on Days 1 and 2. No other clinical signs were observed.

_____: Two mice were found dead, one on Day 1 and the other on Day 14. The mouse found dead on Day 14 exhibited staggering step, reduced motor activity, dyspnea, palpebral ptosis, and was cold to touch for several days. Two mice surviving to study termination exhibited tremors, hunched posture or staggering step, and piloerection on Day 1 and reduced motor activity on Days 2, 3, and 4.

_____: All mice survived. Hunched posture, staggering step, and reduced motor activity were observed in all of the mice on the day of dosing only.

_____: Four of five mice died. Piloerection, hunched posture, prostration, and reduced motor activity were observed in several mice on several occasions prior to death.

SUPPORT INFORMATION OF CONFIDENTIALITY CLAIMS

1. Claims of confidentiality are being made on behalf of RPAC.

2. RPAC asserts this claim of confidentiality until such time as a specific chemical is approved for use in the United States. In the event that the chemicals are never approved, RPAC asserts that the CBI information should be provided permanent protection. The structures and use of the chemicals are unique. Disclosure of this information would provide our competitors with information on facets of our business that would be detrimental to our competitive position.

3. The information claimed as confidential has not been previously disclosed to any other governmental agency or to EPA.

4. This information has been disclosed to only a very limited number of investigators outside of RPAC who have performed either toxicity or efficacy testing. These individuals operate under a strict secrecy agreement. Any individuals who may work with the chemicals will have all health/toxicology information disclosed to them as well, but only on the basis of strict secrecy and respect for the CBI nature of the information.

5. Any individuals to whom the CBI is revealed are warned of the nature of the information. Further, they are informed of their obligations to maintain secrecy should they terminate their employment with RPAC.

6. None of the information claimed as confidential appears in or is referred to in any advertising or promotional materials for the chemical or the end product containing it, professional or trade publications, or any other media available to the public or to our competitors. Appropriate warnings do appear on safety data sheets, as RPAC considers that individuals who are requested to work with the chemicals have every right to know as much about the chemicals' toxicity as possible. Further, the information is only considered to be CBI with respect to the general public, insofar as our competitors could use the information in an unfairly competitive nature.

7. No previous confidentiality determinations have been made by EPA, other Federal agencies or courts in connection with this information.

8. RPAC believes that disclosure of this information to the general public would be likely to result in substantial harm to its competitive position. Disclosure of the alpha numeric designations and chemical names would provide some competitors with information about the specific chemistry of this area of our research and our business. Further, the type of toxicological testing being reported in the TSCA 8(e) notice would provide competitive information about this chemical's status in the research and development process and, therefore, the time remaining until commercialization.

9. A patent has not been issued for the specific chemical structures. However, the generic chemical structures are covered by a patent that is currently pending.

10. The chemicals are not available commercially. They are in the earliest stages of research and development for pesticide use and are unlikely to be developed into commercial products.

11. We believe that disclosure of the chemical names would allow a competitor to synthesize these chemicals. RPAC has invested a large amount of time and money into research of this particular chemical family, and information on specific chemical structures would harm our competitive position.

12. Disclosure of the chemical structures might reveal information on processes used to synthesize these compounds.

13. CAS numbers for these chemicals have not yet been assigned.

14. Currently, the chemicals are not the subject of FIFRA regulation or reporting.

Further questions regarding this submission may be directed to the undersigned at 919-549-2222.

Sincerely,

Glenn S. Simon, PhD, DABT
Director of Toxicology

Triage of 8(e) Submissions

Date sent to triage: 11-22-96 (NON-CAP) CAP

Submission number: 13626 A TSCA Inventory: Y N (D)

Study type (circle appropriate):

Group 1 - Gordon Cash (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX (SBTOX) SEN (w/NEUR)

Group 3 -HERD (1 copy each)

STOX	CTOX	EPI	RTOX	GTOX
STOX/ONCO	CTOX/ONCO	IMMUNO	CYTO	NEUR

Other (FATE, EXPO, MET, etc.):_____

Notes:

☒ This is the **original** 8(e) submission; refile after triage evaluation.

☐ This **original** submission has been **split**; rejoin after triage evaluation.

☐ Other:

Photocopies Needed for Triage Evaluation

entire document: 0 1 2 3

front section and CECATS: 0 1 2 3

Initials:_____ **Date:**_____

Note to contractors: Separate into 16 records

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # 8EHQ-0496-13626 (S) SEQ. A

TYPE: (INT) SUPP FLWP

SUBMITTER NAME: Rhone-Poulenc Ag Company

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
(0639) REFER TO CHEMICAL SCREENING
0678 CAP NOTICE

VOLUNTARY ACTIONS:
(0401) NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKER/OTHERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP./USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

SUB. DATE: 04/10/96 OTS DATE: 04/15/96 CSRAD DATE: 08/05/96

CHEMICAL NAME: Heterocycles — CAS# confident

INFORMATION TYPE:		P F C	INFORMATION TYPE:		P F C	INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04	0216	EPI/CLIN	01 02 04	0241	IMMUNO (ANIMAL)	01 02 04
0202	ONCO (ANIMAL)	01 02 04	0217	HUMAN EXPOS (PROD CONTAM)	01 02 04	0242	IMMUNO (HUMAN)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04	0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04	0243	CHEM/PHYS PROP	01 02 04
0204	MUTA (IN VITRO)	01 02 04	0219	HUMAN EXPOS (MONITORING)	01 02 04	0244	CLASTO (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04	0220	ECO/AQUA TOX	01 02 04	0245	CLASTO (ANIMAL)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04	0221	ENV. OCCC/REL/FATE	01 02 04	0246	CLASTO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04	0222	EMER INCI OF ENV CONTAM	01 02 04	0247	DNA DAM/REPAIR	01 02 04
0208	NEURO (HUMAN)	01 02 04	0223	RESPONSE REQEST DELAY	01 02 04	(0248)	PROD/USE/PROC	01 02 04
(0209)	NEURO (ANIMAL)	01 02 04	(0224)	PROD/COMP/CHEM ID	01 02 04	0251	MSDS	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04	0225	REPORTING RATIONALE	01 02 04	0299	OTHER	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04	~~0226~~	CONFIDENTIAL	01 02 04			
0212	ACUTE TOX. (ANIMAL)	01 02 04	0227	ALLERG (HUMAN)	01 02 04			
(0213)	SUB ACUTE TOX (ANIMAL)	01 02 04	0228	ALLERG (ANIMAL)	01 02 04			
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04	0239	METAB/PHARMACO (ANIMAL)	01 02 04			
0215	CHRONIC TOX (ANIMAL)	01 02 04	0240	METAB/PHARMACO (HUMAN)	01 02 04			

TRIAGE DATA:	NON-CBI INVENTORY	ONGOING REVIEW	SPECIES	TOXICOLOGICAL CONCERN:	USE:	PRODUCTION:
	YES	YES (DROP/REFER)	MUS	(LOW)	research + development pesticide	
CAS SR	NO	NO (CONTINUE)		(MED)		
	(IN TERMINI)	REFER		(HIGH)		

COMMENTS